

REMARKS/ARGUMENTS.

1. Revised Claims.

Claims 1, 3, 4, and 9-32 are pending in the application. Claims 1, 9, 11, 12, and 17 have been currently amended. Amended claims are submitted in which the subject matter of previous claims 9 and 11 have been cognated into claim 1. Claims 9 and 11 have consequently been canceled. The dependency of dependent claims 10 and 12-13 has been corrected to depend on revised claim 1. Claim 15 has also been canceled, since it is superfluous in that claim 16 covers the same subject matter now that the imaging moiety of claim 1 is limited to being radioactive. No new matter has been added to the claims.

2. Claim Rejections: 35 USC §102.

2.1 Noe (US 6,706,723).

Claims 1, 15, 16, 18 and 26-28 stand rejected as lacking novelty over Noe.

Applicants point out that by inference of their omission in the rejection, claim 9, and dependant claims 10-14 were regarded as novel over Noe. Revised claim 1 now contains the essential features of previous claim 9. Claim 1 is therefore now believed novel over Noe. Claims 15, 16, 18 and 26-28 either depend on or refer to claim 1, and are believed novel for the same reasons. The novelty rejection based on Noe should therefore be withdrawn.

3. Claim Rejections: 35 USC §103.

3.1 Grams, Noe, Carpenter and Mobashery.

Claims 1, 9-16, 18 and 26-28 stand rejected as being obvious over the combination Grams [Biol.Chem., 382, 1277-1285 (2001)] in view of Noe, further in view of Carpenter (US 6,656,448) and Mobashery *et al* (US 6,703,415).

Applicants point out that claim 1 now requires that the radiolabel as attached specifically at the R² substituent of Formula IV. As the Examiner has acknowledged, Grams is silent on radiolabelled compounds for imaging.

The Examiner suggests that the combination of Grams and Noe leads in an obvious manner to the subject matter of the present claims. Applicants respectfully disagree. The teaching of Noe is effectively that any isotope (of different atomic mass to the atoms of the chemical structure of Formula I therein), can be attached at any position. Thus, the purported logical combination of [Grams + Noe] is to the compounds of Grams labeled with:

- (i) non-radioactive isotopes;
deuterium (²H), ¹³C, ³¹P, ¹⁷O and ¹⁸O.
- (ii) radioactive isotopes
tritium (³H), ¹⁴C, ¹⁵N, ³²P, ³³P, ¹⁸F and ³⁶Cl.

[The only specific isotopes taught by Grams at Column 20 lines 24-53].

Grams teaches (Column 20 lines 24-27) that an existing atom of the chemical structure may be changed to a different isotope. The compounds taught by Grams are shown in Table 1 (page 1280 therein) and Table 2 (page 1281 therein). Those compounds contain C, H, O, N etc but do not include fluorine (F) or iodine (I). Hence, the combination cannot lead to such compounds labeled with ^{18}F or ^{123}I , since Grams does not teach the presence of such atoms. Similarly, Noe is silent on the attachment of radiometals so cannot provide the subject matter of imaging moiety (i) of present claim 1.

Hence, for imaging moieties $^{99\text{m}}\text{Tc}$, ^{111}In , ^{64}Cu , ^{67}Cu , ^{67}Ga , ^{123}I and ^{18}F of present claim 1, no combination of [Grams and Noe] can provide that subject matter.

In addition, when the teaching of Noe is combined with the compounds of Grams (see eg. Table 1 p. 1281 therein), that would translate to a vast range of possibilities. Noe teaches such isotopic labelling at any position, including multiple labels (Noe Column 20, line 26). That generates a vast list of possibilities. If ones takes eg. Compound 9 of Grams (Table 2 page 1281 therein) that is $\text{C}_{26}\text{H}_{23}\text{N}_5\text{O}_4$ (58 atoms in total). Applying the teaching of Noe, any of from 1 to 26 of the carbon atoms could be ^{13}C or ^{14}C . The number of possibilities for carbon and isotope ^{13}C alone is thus factorial 26 ($26 \times 25 \times 24 \dots 1$). Similarly, any of from 1 to 23 hydrogen atoms could be ^2H or ^3H ; any of from 1 to 4 oxygen atoms could be ^{17}O or ^{14}O etc. There would be hundreds of thousands of possibilities.

In contrast, the clear teaching of present claim 1 of: (a) a single specific radioisotope; (b) attached at R². Such a selection, from hundreds of thousands of possibilities, cannot be obvious. For this reason, applicants contend that the combination [Grams and Noe] cannot lead in an obvious manner to the subject matter of present claim 1.

As noted previously, the inhibitors of Carpenter and Mobashery are structurally completely different to those of Grams. Those references therefore can remedy the deficiencies of [Grams + Noe], ie. provide the teaching of which specific radioisotopes to label at which specific position.

The obviousness rejection based on Grams/Noe/Carpenter/Mobashery should therefore be withdrawn.

3.2 Grams, Noe, Carpenter, Mobashery and Luthra.

Claim 29 stands rejected in view of Grams/Noe/Carpenter/Mobashery (as per 3.1), in further view of Luthra (US 7,115,249).

The Examiner's logic here is that the features of claim 28 are known from Grams/Noe/Carpenter/Mobashery, and that the additional feature of dependent claim 29 can be found in Luthra.

Applicants contend that logic is no longer valid since claim 28 is non-obvious over the combination of reference – see 3.1 above. The obviousness rejection to claim 29 should therefore also be withdrawn.

CONCLUSION

In view of the remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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